

# Service delivery considerations for the development and implementation of LA ARV formulations

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*What policies are needed to be put in place to ensure access to long-acting therapy for the populations who may benefit most from it?*

## What benefits we expect with transition to LA ARV regimens?

### Drug Regimen Optimization with LA ARVs

- ✓ High **durability** (high resistance barrier even if imperfect adherence)
- ✓ High **convenience** (combined formulations, low burden, longer time dose intervals, minimal interference in lifestyle)
- ✓ **Simple** to use (no additional complexities to store, administer or clinical/lab monitoring)
- ✓ Lower **toxicity** and tolerability
- ✓ Use cross all **populations** (including pregnancy, young children and older people) and in those with co-medications without **dose adjustments**
- ✓ Largely available at lower price (**global access**)

### Service Delivery Optimization with LA ARVs

- ✓ **Longer time intervals** between clinical visits / treatment refills
- ✓ More services at **primary care and community levels**
- ✓ Enhancement of **person-centered approach**: psychosocial support and interventions and the engagement/involvement of peers
- ✓ **Low infrastructure needs**/ minimal programme complexity (treatment initiation and follow up)
- ✓ Promote **equity and integration** with other health programmes
- ✓ **Cost effective / cost saving** intervention

# Challenges and approaches to integrate long acting ARVs into clinic and programmatic framework

Major areas	Key challenges in transitioning to <u>current LAIs</u>	Major concerns	Potential approaches
Clinical/Pharmacological (regimens)	<ul style="list-style-type: none"> <li>• “pK tail”</li> <li>• Drug interactions</li> <li>• Polypharmacy</li> <li>• Pharmacogenetics</li> <li>• Changes in physiologic status (pregnancy, co-infections, changes in body weight)</li> </ul>	<ul style="list-style-type: none"> <li>• Subtherapeutic levels (reduced efficacy, resistance risk),</li> <li>• Need of lead in / dose escalation/adjustments</li> <li>• management of toxicities</li> </ul>	<ul style="list-style-type: none"> <li>• Use of prodrugs</li> <li>• Multiple implants with different dosages (“tunneled”/reservoir in style implants,</li> <li>• Biodegradable implants</li> <li>• LA oral formulations (particularly for elderly patients)</li> <li>• TDM</li> </ul>
Acceptability (formulations)	<ul style="list-style-type: none"> <li>• Injection site pain</li> <li>• Size/ visibility of implants (socio-cultural issues)</li> <li>• Management of adverse events</li> </ul>	<ul style="list-style-type: none"> <li>• Adherence</li> <li>• Stigma</li> <li>• Values and preferences of HCWs /patients (concerns in “switching” treatment)</li> </ul>	<ul style="list-style-type: none"> <li>• SC injections, microneedles (microarray patches),</li> <li>• Implants (synergies with contraceptives/other disease treatments - neuropsychiatric disorders),</li> <li>• Nano formulations (low volumes)</li> <li>• Implementation studies in more diverse settings</li> </ul>
Operational (logistics for stock, drug application and patient follow up)	<ul style="list-style-type: none"> <li>• Service/programme SOPs changes from an oral to injectable treatment platform</li> <li>• Cost-effectiveness/ cost savings ( high cost)</li> </ul>	<ul style="list-style-type: none"> <li>• IM supply costs</li> <li>• privacy space in services for injection</li> <li>• stock/ refrigeration needs,</li> <li>• HCW training needs,</li> <li>• service visit schedules, waste disposal</li> </ul>	<ul style="list-style-type: none"> <li>• Use of non-traditional health care models (pharmacies, minute clinics, community-based organizations, mobile vans, home visits),</li> <li>• Extension of dose intervals</li> <li>• Heat stable formulations all components of the regimen,</li> <li>• Biosafety measures with needles and syringes</li> <li>• CE /benefit analysis in different populations</li> </ul>

# CAB/RPV as proof of concept for LA ARVs: advantages & (many) challenges



## CAB/RPV: advantages

- High virologic suppression rates (non-inferior to oral TLD)
- Low toxicity/side effects (local reactions)
- Good tolerability/acceptability (mainly in high income settings)
- Can be taken every 1-2 months (instead daily oral tablets)
- Approved use for maintenance in adherent patients (suppressed VL)
- May be most appropriate for high income settings (good infrastructure)

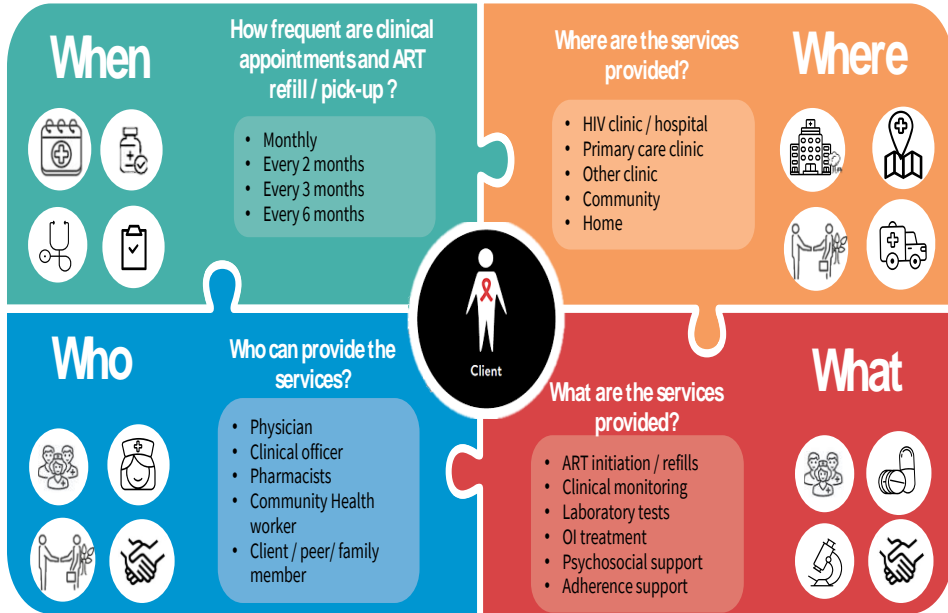
## CAB/RPV: challenges

- Not approved for use in pregnant women /breastfeeding women and children (limited data)
- Not active against HBV and cannot be used in TB coinfection (interactions with rifampin)
- Potential for resistance in non-adherent patients
- Limited safety and efficacy data in LMICs (high prevalence of NNRTI resistance)
- **Administration challenges:** requires oral lead in dose and IM injections (2 injections, large volume, not self administered)
- **Delivery challenges:** cold chain required(RPV) ; private place needed for IM injections & HCW training
- **Visit challenges:** Need monthly visits (contrast with 3-6 monthly visits recommended for TLD)



The goal of DSD is to decrease barriers in access to care and to guarantee the quality of services at reasonable costs to the health care system

# The impact of transitioning to LA ARVs on building blocks of DSD for HIV treatment



## Adoption of WHO public health approach to HIV programmes

- Standardization
- Simplification
- Decentralization
- Equity
- Integration into UHC

DSD building block	Current DSD model (oral cART - TLD)	Current LAI management (injectable CAB/RPV)	Optimized DSD model (future LAIs)
<b>WHEN:</b> frequency of treatment refills and clinical appointment	3-6 monthly drug pickup 6 monthly clinical visits	<b>1-2 monthly IM injections and clinical visits</b> (need of oral lead dosing, 2 separate injections, not self administered)	6-12 monthly injections (SC self injections/implants) 6-12 monthly clinical visits
<b>WHERE:</b> Where are the service provided	HIV clinic/hospital (decentralizing to primary care/outreach services)	<b>HIV clinic/hospital</b> (infrastructure for IM injecting, cold chain for RPV, management of syringes and needles)	Use of non-traditional health care models (pharmacies, minute clinics, community-based organizations, mobile vans, home visits)
<b>WHO:</b> Who can provide the services	ART prescription by trained HCWs ART dispensing by HCWs task sharing with trained primary health/ community health care workers	ART prescription and dispensing (IM injection ) by <b>trained HCW</b>	ART prescription in HIV clinic/primary care /community /mobile/home services (with referral system) SC self -injection / implant
<b>WHAT:</b> What are the services	ART prescription & refills, clinical & lab monitoring, OI/comorbs management, psychosocial & adherence support	Same as current DSD +IM <b>injecting sites (+logistics)</b>	Same as current DSD + SC self injection/implant (strong community support)

# Adapting DSD models to inclusion of future long-acting ARVs

Intervention	DSD model	DSD intervention description	What should be adapted for DSD models in optimized LAI context
Adherence clubs (AC)—clinic and community-based	Health care worker managed groups	Group on established ART led by a HCW /peer meets every 2–3 months within /out facility for <b>group counseling and ART refill</b>	<ul style="list-style-type: none"> <li>• Longer intervals for drug refill and clinical consultations in patients established on ART (every 6-12 months).</li> <li>• Group counselling activities more focused on psychosocial support and engagement of peers (every 3 months ? - can be shorter depending on the community based activity package)</li> </ul>
Community ART groups (CAG)	Client managed groups	Self-formed groups on established ART living in same area, meets monthly within the community for <b>group counseling and ART refill</b> . One member visits the clinic monthly to collect ART refill for the group and clinical consultation on rotational basis (each member visits the clinic at <b>least once every 6-months</b> )	
Community ART refill groups (CARG)	Client managed groups	Self-formed groups ART patients living in same community, meets for <b>group counseling</b> . One member visit clinic <b>every 3-months</b> to clinical consultation, (group visits the clinic for annual consultation).	
Community drug distribution points/decentralized medication delivery (CDDP/DMD)	Community based individual model	Peer-led centers within the community where established on ART come for <b>3-monthly ART refills with 1-yearly clinical consultation</b> at the facility	
Down-referral (DR)	Facility based individual model	<b>Referral of patients established on ART</b> from secondary health facilities to primary health centers for the continuation of care, one of the first models tried.	<ul style="list-style-type: none"> <li>• Referral from secondary/primary health centers to community level as preferred approach</li> <li>• Integration with NCDs/ SRH and other programmes</li> </ul>
Home delivery (HD)	Community based individual model	<b>Monthly delivery of ART by community care workers to patients at home</b> or any other location within the community	<ul style="list-style-type: none"> <li>• Home visits in specific circumstances for drug delivery/ implant check/clinical follow up</li> </ul>
Multimonth scripting (MMS)	Facility based individual model	<b>Three-monthly clinical consultation with drug refill</b> at the health facility	<ul style="list-style-type: none"> <li>• 6-12 monthly refill (SC injections) and 6 monthly clinical consultations/ implant check</li> <li>• Inclusion of drug refill of injectable formulations (SC) and implant check in outreach programme</li> </ul>
Six monthly appointment/fast track refill (SMA/FTR)	Facility based individual model	<b>Six-monthly clinical consultation with 3-monthly ART refill</b> by CHW	
Outreach (OR)	Community based individual model	ART <b>drug refill integrated into existing outreach programs</b> held in the community	

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